REMARKS

Introduction

Receipt of the Office Communication dated May 20, 2003 is acknowledged. Applicants have made the clean copy of the amendments consistent with the marked-up version of the claims. Prior to the present amendments, Claims 1-18 were pending in the application. Claims 1, 2, 17, and 18 have been amended. New claims 19 and 20 have been added. Support for the new claims can be found throughout the specification (specification page 7, lines 3-4).

Claims 1-20 are now pending. Applicants respectfully request entry of the proposed amendments, since no new matter has been introduced.

Rejections Based on 35 USC § 102(b)

A schematic figure of the method for preparing a fiber mutant adenovirus vector of the present invention and that of the Dmitriev reference is shown in the attached sheet. Based on this attached figure, applicants explain below the difference between the present invention and the Dmitriev *et al.*

In the method for preparing a fiber mutant adenovirus vector of the Dmitriev *et al.* reference, at first, an oligonucleotide encoding the polypeptide of interest is introduced into a shuttle vector (a plasmid possessing only a fiber coding region), and next, the modified fiber having an altered fiber region is cut out and then introduced into an adenovirus genome by homologous recombination using a special strain of *Escherichia coli* (BJ5TS3). Since a special strain of *Escherichia coli* (BJ5183) is used in the homologous recombination, re-transformation into the standard strain of Escherichia coli (DH5 a) is required as a final step for the preparation of plasmid.

That is, in Dmitriev *et al.* a procedure comprising the above three steps must be conducted to obtain an adenovirus vector into which the polypeptide encoding the desired peptide is introduced. The procedure is very complicated.

According to the present invention, by contrast, an oligo DNA encoding the polypeptide of interest is introduced into a nucleotide sequence encoding the HI loop of the fiber using restriction enzyme recognition sequences which are not originally present in adenovirus genomic DNA (for example, Csp4S and/or CiaI). Thus, an oligo DNA that encodes the polypeptide of interest can be introduced into the adenovirus genome in only one step, whereby the preparation of a vector is simplified remarkably. In addition, the method of the present invention does not require homologous recombination using a special strain of Escherichia coli (BJ5183) as in Dmitriev *et al.*, but only requires in vitro ligation, which is the most fundamental technique.

Accordingly, the present invention is utterly different from that of Dmitriev *et al.*, and should not be rejected under 35 U.S.C. § 102(b).

Rejections Based on 35 USC § 103

Dmitriev *et al.* contains no description to the effect that oligo DNA encoding the polypeptide of interest is introduced directly into a fiber HI loop of the adenovirus genome, and that restriction enzyme recognition sequences are employed that are not originally present in adenovirus genomic DNA.

In Arap *et al.*, moreover, there is nothing that discloses or suggests that oligo DNA encoding the polypeptide of interest is directly introduced into a fiber HI loop of the adenovirus genome. Also, nothing in the reference implicates the use of restriction enzyme recognition sequences that are not present in adenovirus genomic DNA originally. Arap *et al.* only teaches that NGR peptide is more effective for tumor homing.

Accordingly, the method of the present invention does not follow from any of the references. As described above, furthermore, the presently recited step in the method can be simplified as compared with the conventional methodology for preparing a fiber mutant adenovirus vector as disclosed in Dmitriev *et al.* This remarkable effect was obtained with the present invention for the first time and could not have been expected from any of the references.

From the foregoing, the present invention is not rendered obvious by any combination of Dmitriev *et al.* and Arap *et al.*, and should not be rejected under 35 U.S.C. § 103.

CONCLUSION

In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions, the Examiner is courteously invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

MARKED UP VERSION OF CLAIMS SHOWING CHANGES MADE

1. (**Amended**) A method for constructing a fiber-mutant adenovirus vector which comprises the steps of inserting [~~a unique restriction enzyme recognition sequence~~] **a restriction enzyme recognition sequence which is not originally present in adenovirus genomic DNA** into a fiber HI loop-coding gene sequence, and introducing a foreign peptide-coding DNA into the gene sequence.

2. (**Amended**) The method according to claim 1 wherein [~~the unique restriction enzyme~~] **the restriction enzyme recognition sequence which is not originally present in adenovirus genomic DNA** is *Csp*451 and/or *Cla*I.

17. (**Amended**) An adenovirus vector which comprises [~~a unique restriction enzyme~~] **a restriction enzyme recognition sequence which is not originally present in adenovirus genomic DNA** site in the fiber HI loop-coding gene sequence.

18. (**Amended**) The adenovirus vector according to claim 17 wherein [~~the unique restriction enzyme~~] **the restriction enzyme recognition sequence which is not originally present in adenovirus genomic DNA** is *Csp*451 and/or *Cla*I.